

Applicants: Peter S. Linsley, et al.
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Please amend the subject application as follows:

In the claims:

In compliance with the practice guidelines for making amendments, Applicants present all pending claims with status indicators and submit new claims 29-30.

1. (Withdrawn) A soluble CTLA4 mutant molecule having the extracellular domain of CTLA4 which binds CD80 or CD86.
2. (Withdrawn) The soluble CTLA4 mutant molecule of claim 1, wherein the extracellular domain of CTLA4 comprises one or more mutations in a region S25-R33 of CTLA4 of Figure 3 (SEQ ID NO:2, at positions 51-59), and wherein the mutation is a substitution of any amino acid beginning with serine at position +25 of Figure 3 (SEQ ID NO:2, at position 51) and ending with arginine at position +33 of Figure 3 (SEQ ID NO:2, at position 59) with a different amino acid selected from alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, and valine.
3. (cancelled)
4. (cancelled)
5. (Withdrawn) The soluble CTLA4 mutant molecule of claim 1, wherein the extracellular domain of CTLA4 comprises one or more mutations in a region E95-G107 of CTLA4 of Figure 3 (SEQ ID NO:2, at positions 121-133), and wherein the mutation is a substitution of any amino acid beginning with glutamic acid at position +95 of Figure 3 (SEQ ID NO:2, at position 121) and ending with glycine

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at position +107 of Figure 3 (SEQ ID NO:2, at position 133) with a different amino acid selected from alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, and valine.

6. (cancelled)
7. (cancelled)
8. (cancelled)
9. (Withdrawn) The soluble CTLA4 mutant molecule of claim 1, wherein the extracellular domain of CTLA4 comprises one or more mutations in a region N108-I115 of CTLA4 of Figure 3 (SEQ ID NO:2, at positions 134-141), and wherein the mutation is a substitution of any amino acid beginning with asparagine at position +108 of Figure 3 (SEQ ID NO:2, at position 134) and ending with isoleucine at position +115 of Figure 3 (SEQ ID NO:2, at position 141) with a different amino acid selected from a group consisting of alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, and valine.
10. (cancelled)
11. (Withdrawn) The soluble CTLA4 mutant molecule of claim 1 further comprising an amino acid sequence which alters the solubility, affinity or valency of the soluble CTLA4 mutant molecule for binding to CD80 or CD86.

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12. (Withdrawn) The soluble CTLA4 mutant molecule of claim 11, wherein the amino acid sequence comprises a human immunoglobulin constant region.
13. (Withdrawn) A nucleic acid molecule comprising a nucleotide sequence encoding the amino acid sequence corresponding to the soluble CTLA4 mutant molecule of claim 1.
14. (Withdrawn) A vector comprising the nucleotide sequence of claim 13.
15. (Withdrawn) A host vector system comprising the vector of claim 14 in a suitable host cell.
16. (Withdrawn) The host vector system of claim 15, wherein the suitable host cell is a prokaryotic cell or a eukaryotic cell.
17. (Withdrawn) A method for producing a soluble CTLA4 mutant protein comprising growing the host vector system of claim 16 so as to produce the protein in the host cell and recovering the protein so produced.
18. (Withdrawn) A soluble CTLA mutant protein produced by the method of claim 17.
19. (Withdrawn) A method for regulating a T cell interaction with a CD80 and/or CD86 positive cell comprising contacting the CD80 and/or CD86 positive cell with the soluble CTLA4 mutant molecule of claim 1 so as to regulate the T cell interaction.
20. (Withdrawn) The method of claim 19, wherein the soluble CTLA4 mutant molecule is any of L104EA29L (SEQ ID NO.: 16), L104EA29T (SEQ ID NO.: 18), or L104EA29W (SEQ ID NO.: 20).

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21. (Withdrawn) The method of claim 19, wherein the CD80 and/or CD86 positive cell is an antigen presenting cell.
22. (Withdrawn) The method of claim 19, wherein the interaction of the CTLA4-positive T cells with the CD80 and CD86 positive cells is inhibited.
23. (Withdrawn) A method for treating immunoproliferative diseases mediated by T cell interactions with B7 positive cells comprising administering to a subject the soluble CTLA4 mutant molecule of claim 1, in an amount effective to regulate T cell interactions with said B7 positive cells.
24. (Withdrawn) The method of claim 23, wherein said T cell interactions are inhibited.
25. (Withdrawn) The method of claim 23, wherein the immunoproliferative disease is graft versus host disease.
26. (Withdrawn) The soluble CTLA4 mutant molecule of claim 1, wherein the extracellular domain of CTLA4 comprises amino acid residues from about position 93 to about position 124 of Figure 3 (SEQ ID NO:2 beginning at position 119 and ending at position 150) joined to amino acid residues from about position 1 to about position 94 of the amino acid sequence corresponding to the extracellular domain of CD28.
27. (Withdrawn) The soluble CTLA4 mutant molecule of claim 1, wherein in the extracellular domain of CTLA4, the second proline in the amino acid motif MYPPPY (SEQ ID NO:35) is replaced with alanine.

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28. (Withdrawn) The soluble CTLA4 mutant molecule of claim 1, wherein the extracellular domain of CTLA4 comprises:

- a. one or more mutations in a region S25-R33 of CTLA4 of Figure 3 (SEQ ID NO.: 2, at positions 51-59), and wherein the mutation is a substitution of any amino acid beginning with serine at position +25 of Figure 3 (SEQ ID NO.: 2, at position 51) and ending with arginine at position +33 of Figure 3 (SEQ ID NO.: 2, at position 59) with a different amino acid selected from alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, and valine; and
- b. one or more mutations in a region E95-G107 of CTLA4 of Figure 3 (SEQ ID NO.: 2, at positions 121-133), and wherein the mutation is a substitution of any amino acid beginning with glutamic acid at position +95 of Figure 3 (SEQ ID NO.: 2, at position 121) and ending with glycine at position +107 of Figure 3 (SEQ ID NO.: 2, at position 133) with a different amino acid selected from alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, and valine.

Please add new claims 29-30 as follows:

- 29. (New) A CTLA4Ig fusion protein reactive with B7 antigen and encoded by DNA deposited as ATCC 68629.--
- 30. (New) A CTLA4Ig fusion protein having the amino acid sequence of a CTLA4Ig fusion protein expressed by the cell deposited as ATCC 10762, wherein said CTLA4Ig fusion protein is reactive with B7 antigen.